Serial No.: 09/407,605

Filed: September 28, 1999

Page : 2 of 11

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

**Listing of Claims:** 

1-80. (Canceled)

81. (Previously Presented) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of at least 150 codons all of which are common codons, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

- 82. (Previously Presented) The synthetic nucleic acid sequence of claim 81 where the factor VIII protein has one or more of the following characteristics:
  - a) the B domain is deleted (beta domain deleted (BDD) factor VIII);
  - b) it has a recognition site for an intracellular protease of the PACE/furin class; or
  - c) it is expressed in a non-transformed cell.
- 83. (Previously Presented) The synthetic nucleic acid sequence of claim 81, wherein the number of non-common or less-common codons replaced or remaining is between one and 15.
- 84. (Previously Presented) The synthetic nucleic acid sequence of claim 81, wherein all non-common and less-common codons are replaced with common codons.

Serial No.: 09/407,605

Filed: September 28, 1999

Page : 3 of 11

85. (Previously Presented) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence, wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

- 86. (Previously Presented) The synthetic nucleic acid sequence of claim 85 where the factor VIII protein has one or more of the following characteristics:
  - a) the B domain is deleted (BDD factor VIII);
  - b) it has a recognition site for an intracellular protease of the PACE/furin class; or
    - c) it is expressed in a non-transformed cell.
- 87. (Previously Presented) The synthetic nucleic acid sequence of claim 85, wherein the number of non- common or less- common codons replaced or remaining is between one and 15.
- 88. (Previously Presented) The synthetic nucleic acid sequence of claim 85, wherein all non-common and less-common codons are replaced with common codons.
- 89. (Previously Presented) A synthetic nucleic acid sequence which encodes human Factor VIII or a functional portion thereof, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein at least 98% or more of the codons in the sequence encoding the Factor VIII are common codons and the Factor VIII is at least 90 amino acid residues in length, and wherein by a common codon is meant the most common codon

Serial No.: 09/407,605

Filed: September 28, 1999

Page : 4 of 11

encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

90. (Previously Presented) The synthetic nucleic acid sequence of claim 89 where the factor VIII protein has one or more of the following characteristics:

- a) the B domain is deleted (BDD factor VIII);
- b) it has a recognition site for an intracellular protease of the PACE/furin class; and
- c) it is expressed in a non-transformed cell.
- 91. (Previously Presented) The synthetic nucleic acid sequence of claim 89, wherein the number of non- common or less- common codons replaced or remaining is between one and 15.
- 92. (Previously Presented) The synthetic nucleic acid sequence of claim 89, wherein the number of non-common or less-common codons replaced or remaining, taken together, are equal or less than 2% of the codons in the synthetic nucleic acid sequence.
- 93. (Previously Presented) The synthetic nucleic acid sequence of claim 89, wherein all non-common and less-common codons are replaced with common codons.
- 94. (Previously Presented) The synthetic nucleic acid sequence of claim 89, wherein at least 99% of the codons in the synthetic nucleic acid sequence are common codons.
  - 95. (Canceled)
- 96. (Previously Presented) The synthetic nucleic acid sequence of claim 89, wherein all of the codons are replaced with common codons.

Serial No.: 09/407,605

Filed: September 28, 1999

Page : 5 of 11

97. (Previously Presented) A synthetic nucleic acid sequence which encodes human Factor IX, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of at least 150 codons all of which are common codons, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.

- 98. (Previously Presented) The synthetic nucleic acid sequence of claim 97, wherein the Factor IX protein has one or more of the following characteristics:
  - a) it has a PACE/furin site at a pro-peptide mature protein junction; and
  - b) is expressed in a non-transformed cell.
- 99. (Previously Presented) The synthetic nucleic acid sequence of claim 97, wherein the number of non- common or less- common codons replaced or remaining is between one and 15.
- 100. (Previously Presented) A synthetic nucleic acid sequence which encodes human Factor IX, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein the synthetic nucleic acid has a continuous stretch of common codons which comprise at least 60% of the codons of the synthetic nucleic acid sequence, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.
- 101. (Previously Presented) The synthetic nucleic acid sequence of claim 100, wherein the number of non- common or less- common codons replaced or remaining is between one and 15.

Serial No.: 09/407,605

Filed: September 28, 1999

Page : 6 of 11

102. (Previously Presented) The synthetic nucleic acid sequence of claim 100, wherein the factor IX protein has one or more of the following characteristics:

- a) it has a PACE/furin site at a pro-peptide mature protein junction; and
- b) is expressed in a non-transformed cell.
- 103. (Previously Presented) A synthetic nucleic acid sequence which encodes human Factor IX, wherein at least one non-common codon or less-common codon has been replaced by a common codon encoding the same amino acid residue as the non-common or less-common codon and wherein at least 98% or more of the codons in the sequence encoding the Factor IX are common codons and the Factor IX is at least 90 amino acid residues in length, and wherein by a common codon is meant the most common codon encoding each particular amino acid residue in highly expressed human genes as shown in Figure 14A-B.
- 104. (Previously Presented) The synthetic nucleic acid sequence of claim 103, wherein the factor IX protein has one or more of the following characteristics:
  - a) it has a PACE/furin site at a pro-peptide mature protein junction; and
  - b) is expressed in a non-transformed cell.
- 105. (Previously Presented) The synthetic nucleic acid sequence of claim 103, wherein the number of non- common or less- common codons replaced or remaining is between one and 15
- 106. (Previously Presented) The synthetic nucleic acid sequence of claim 103, wherein the number of non-common or less-common codons replaced or remaining, taken together, are equal or less then 2% of the codons in the synthetic nucleic acid sequence.

Serial No.: 09/407,605

Filed: September 28, 1999

Page : 7 of 11

107. (Previously Presented) The synthetic nucleic acid sequence of claim 103, wherein all non- common and less-common codons are replaced with common codons.

108. (Previously Presented) The synthetic nucleic acid sequence of claim 103, wherein at least 99% of the codons in the synthetic nucleic acid sequence are common codons.

## 109. (Canceled)

- 110. (Previously Presented) The synthetic nucleic acid sequence of claim 103, wherein all of the codons are replaced with common codons.
- 111. (Currently Amended) A vector comprising the synthetic nucleic acid sequence of claim 64, 69, or 73 81, 85, 89, 97, 100 or 103.
- 112. (Currently Amended) A cell comprising the nucleic acid sequence of claim 64, 69, or 73-81, 85, 89, 97, 100 or 103.

113-135. (Canceled)